

AMENDMENTS TO THE CLAIMS

This listing of claims replaces all previous versions, and listings, of claims in this application.

1. (Canceled)
2. (Previously Presented) The method according to claim 59, wherein the composition comprises a sufficient amount of at least one release-rate modifier to provide a modified release of the tacrolimus sufficient to provide a dissolution rate in vitro of the composition, which when measured according to USP dissolution test (paddle) employing water as dissolution medium, 100 rpm and a temperature of about 37 °C permits release of less than 85% w/w within about 30 min after start of the test.
3. (Previously Presented) The method according to claim 2, wherein less than about 80% w/w is released within about 30 min after start of the test.
4. (Previously Presented) The method according to claim 2, wherein less than 85% w/w is released within about 6 hours after start of the test.
5. (Previously Presented) The method according to claim 4, wherein less than 80% w/w is released within the first hour after start of the test.
6. (Previously Presented) The method according to claim 4, wherein less than 80% w/w is released within 2 hours after start of the test.
7. (Previously Presented) The method according to claim 4, wherein less than 80% w/w is released within 3 hours after start of the test.
8. (Previously Presented) The method according to claim 4, wherein less than 80% w/w is released within 6 hours after start of the test.

9. (Previously Presented) The method according to claim 2, wherein less than 75% w/w is released within about 10 hours after start of the test.
10. (Previously Presented) The method according to claim 9, wherein less than 70% w/w is released within about 10 hours after start of the test.
11. (Previously Presented) The method according to claim 9, wherein more than 20% w/w within about 10 hours after start of the test.
12. (Previously Presented) The method according to claim 2, wherein more than 20% w/w is released within about 15 hours after start of the test.
13. (Previously Presented) The method according to claim 59, wherein the composition comprises a sufficient amount of at least one release-rate modifier so that, when the composition is ingested by a mammal, the active substance is released in the gastrointestinal tract of the mammal at a rate so that less than 85% w/w is released within the first 30 min after ingestion.
14. (Previously Presented) The method according to claim 13, wherein less than about 80% w/w is released within about 30 min after ingestion.
15. (Previously Presented) The method according to claim 13, wherein less than 85% w/w is released within about 6 hours after ingestion.
16. (Previously Presented) The method according to claim 15, wherein less than 80% w/w is released within the first hour after ingestion.
17. (Previously Presented) The method according to claim 15, wherein less than 80% w/w is released within 2 hours after ingestion.
18. (Previously Presented) The method according to claim 15, wherein less than 80% w/w is released within 3 hours after ingestion.

19. (Previously Presented) The method according to claim 15, wherein less than 80% w/w is released within 6 hours after ingestion.
20. (Previously Presented) The method according to claim 13, wherein less than 75% w/w is released within about 7 hours after ingestion.
21. (Previously Presented) The method according to claim 20, wherein less than 70% w/w or less than about 65% w/w is released within about 7 hours after ingestion.
22. (Previously Presented) The method according to claim 13, wherein more than 20% w/w within about 10 hours after ingestion.
23. (Previously Presented) The method according to claim 13, wherein more than 20% w/w is released within about 24 hours after ingestion.
- 24-35. (Canceled)
36. (Previously Presented) A method according to claim 59, wherein the particles obtained have a geometric weight mean diameter d_{gw} of $\geq 10 \mu\text{m}$.
- 37-38. (Canceled)
39. (Previously Presented) The method according to claim 59, wherein the method is carried out in a high or low shear mixer or in a fluid bed.
40. (Previously Presented) The method according to claim 59, wherein the process is carried out in a fluid.
41. (Previously Presented) The method according to claim 59, wherein the spraying is performed through a spraying device equipped with temperature controlling means.
42. (Canceled)

43. (Previously Presented) The method according to claim 59, wherein the concentration of the oily material in the particulate material is from about 5 to about 95% v/v.
44. (Canceled)
45. (Previously Presented) The method according to claim 59, wherein the first composition in liquid form has a viscosity (Brookfield DV-III) of at most 800 mPas at a temperature of at the most 100 °C.
46. (Previously Presented) The method according to claim 59, wherein the first composition is essentially non-aqueous and it contains at most 20% w/w water.
47. (Previously Presented) The method according to claim 59, wherein the oily material has a melting point of at least 30 °C.
48. (Previously Presented) The method according to claim 59, wherein the oily material has a melting point of at most 300 °C.
49. (Previously Presented) The method according to claim 59, wherein the first composition comprises one or more pharmaceutically acceptable excipients.
50. (Previously Presented) The method according to claim 59, wherein the second composition comprises one or more pharmaceutically acceptable excipients.
51. (Previously Presented) The method according to claim 49, wherein the pharmaceutically acceptable excipient is selected from the group consisting of fillers, binders, disintegrants, glidants, colouring agents, taste-masking agents, pH-adjusting agents, solubilizing agents, stabilising agents, wetting agents, surface active agents, and antioxidants.
52. (Canceled)
53. (Previously Presented) The method according to claim 59, wherein the tacrolimus is dispersed in the first composition.

54. (Previously Presented) The method according to claim 59, further comprising a step of processing the particles obtained optionally together with one or more pharmaceutically acceptable excipients into a solid dosage form.

55. (Previously Presented) The method according to claim 54, wherein the solid dosage form is selected from the group consisting of tablets, capsules and sachets.

56. (Previously Presented) The method according to claim 54, wherein the solid dosage form is provided with a coating.

57. (Previously Presented) The method according to claim 56, wherein the coating is selected from the group consisting of film-coatings, modified release coatings, enteric coatings, sugar coatings and taste-masking coatings.

58. (Canceled)

59. (Previously Presented) A method for preparing a solid composition comprising tacrolimus and a release-rate modifier, the method comprising the steps of

i) selecting a first composition comprising an oily material having a melting point of at least 5 °C, wherein the first composition comprises a mixture of polyethylene glycol having an average molecular weight of from 3,000 to 35,000 and poloxamer;

ii) optionally bringing the first composition into liquid form,

iii) dispersing or dissolving tacrolimus in the liquid first composition at a temperature below the melting point of the tacrolimus,

iv) spraying the resulting first composition onto a solid second composition having a temperature below the melting point of the first composition,

v) adding at least one release-rate modifier to the resulting composition by dry mixing,

vi) mechanically working the resulting composition to obtain particles, and

vii) optionally subjecting the particulate material to conventional methods for preparing solid dosage forms.

60-65. (Canceled)

66. (Previously Presented) A solid composition prepared by the method of claim 59.

67-70. (Canceled)

71. (Previously Presented) The method according to claim 59, wherein the solid second composition comprises lactose.

72. (Canceled)

73. (Previously Presented) The method according to claim 59, wherein the first composition comprises PEG6000 and poloxamer 188.

74. (Canceled)

75. (Previously Presented) The method according to claim 59, wherein the release-rate modifier is hydroxypropyl methylcellulose.

76. (Canceled)

77. (Previously Presented) The method according to claim 73, wherein the release-rate modifier is hydroxypropyl methylcellulose.

78.-79. (Canceled)

80. (Currently Amended) The method according to claim 59 77, wherein the polyethylene glycol, poloxamer, and hydroxypropyl methylcellulose form a matrix.

81. (Previously Presented) The method according to claim 59, wherein the concentration of release-rate modifier is from about 10 to about 60% w/w.

82. (Currently Amended) The method according to claim 59 75, wherein the concentration of release-rate modifier is from about 10 to about 60% w/w.

83. (Canceled)

84. (Previously Presented) A solid composition prepared by the method of claim 73.

85. (Canceled)

86. (Previously Presented) A method for preparing a solid dosage form comprising tacrolimus, the method comprising the steps of

i) dispersing or dissolving tacrolimus in a liquid first composition at a temperature below the melting point of the tacrolimus, wherein the first composition comprises (i) polyethylene glycol having an average molecular weight of from 3,000 to 35,000 and (ii) poloxamer;

ii) spraying the resulting first composition onto a solid second composition having a temperature below the melting point of the first composition,

iii) adding hydroxypropyl methylcellulose and optionally additional release-rate modifiers to the product of step (ii),

iv) forming a solid dosage form from the product of step (iii), wherein the solid dosage form comprises from about 10 to about 60% w/w of hydroxypropyl methylcellulose.

87. (Previously Presented) The method according to claim 86, wherein the hydroxypropyl methylcellulose is added in a fluid bed.

88. (Previously Presented) The method according to claim 86, wherein the polyethylene glycol, poloxamer, and hydroxypropyl methylcellulose form a matrix.

89. (Previously Presented) The method according to claim 86, wherein the solid dosage form is a tablet.

90. (Previously Presented) A solid dosage form prepared by the method of claim 86.